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Prognostic factors in metastasectomy of lung metastases from colorectal cancer

Kolorektal kanser akciğer metastazlarının metastazektomisinde prognostik faktörler

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ABSTRACT

Background: This study aims to evaluate prognostic factors on survival in pulmonary metastases of colorectal cancers.

Methods: In this single-center study, 33 patients (17 males, 16 females; mean age 55.6 years) who underwent metastasectomy due to lung metastases of colorectal cancer in our clinic between March 1998 and June 2011 were retrospectively analyzed. The prognostic factors associated with survival were investigated.

Results: The median survival of the patients was 74 months (range 6 to 99 months) and five-year survival rate was 62%. The median, one, three, and five-year survival rates were 49 months, 94%, 70%, and 33% in males respectively, while the corresponding figures for female patients were 92 months, 100%, 89%, and 89%, respectively (p=0.001). In patients with a pre-thoracotomy carcinoembryonic antigen (CEA) level below 5 ng/mL, one, three and five-year survival rates were 100%, 89%, and 75% respectively, while the corresponding figures for those patients with a CEA level above 5 ng/mL were 83%, 42%, and 0%, respectively (p=0.001).

Conclusion: Although metastasectomy is associated with improved survival in lung metastases of colorectal cancer, prognostic factors have not been fully elucidated. Our findings suggest that female gender and a preoperative CEA level below 5 ng/mL are more eligible candidates for metastasectomy.

Keywords: Chest surgery; colorectal carcinom; metastasectomy.

ÖZ

Amaç: Bu çalışmada kolorektal kanserlerin akciğer metastazlarında prognostik faktörlerin sağkalıma etkisi araştırıldı.

Çalışma planı: Bu tek merkezli çalışmada kliniğimizde Mart 1998 - Haziran 2011 tarihleri arasında kolorektal kanserin akciğer metastazı nedeni ile metastazektomi uygulanan ve tüm kayıtlarına ulaşılabilen 33 hasta (17 erkek, 16 kadın; ort. yaş 55.6 yıl) retrospektif olarak incelendi. Sağkalım ile ilişkili prognostik faktörler araştırıldı.

Bulgular: Hastaların medyan sağkalım süresi 74 ay (dağılım 6-99 ay) iken beş yıllık sağkalım oranı %62 idi. Erkeklerde medyan sağkalım ve bir, üç ve beş yıllık sağkalım oranları 49 ay ve %94, %70 ve %33 iken, kadın hastalarda sırasıyla 92 ay ve %100, %89 ve %89 olarak saptandı (p=0.001). Torakotomi öncesi ölçülen karsinoembriyonik antijen (CEA) düzeyi 5 ng/mL'nin altında olan hastalarda bir, üç ve beş yıllık sağkalım oranları sırasıyla %100, %89 ve %75 iken, CEA düzeyi 5 ng/mL'nin üzerinde olan hastalarda bu oran sırasıyla %83, %42 ve %0 idi (p=0.001).

Sonuç: Akciğerin kolorektal kanser metastazlarında metastazektomi ile sağkalım süresi uzatılabilmekte, ancak prognostik faktörler kesin olarak bilinmemektedir. Çalışma bulgularımız, kadın cinsiyeti ve ameliyat öncesi CEA düzeyi 5 ng/mL'nin altında olan hastaların metastazektomi için daha uygun aday olduğunu düşündürmektedir.

Anahtar sözcükler: Göğüs cerrahisi; kolorektal karsinom; metastazektomi.

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The lung is a common site of metastasis from various cancers, and patients with lung metastases have an unfavorable prognosis. Lung and liver metastases occur in more than half of the patients who undergo resection for colorectal cancer. Left untreated, these metastases are known to be associated with an average survival rate of approximately 10 months and a five-year survival rate of less than 5%.[1-3]

Many studies have shown that metastasectomies in appropriately selected cases may improve the chance of survival for patients with different primary tumors. In addition, there has been limited data suggesting that metastasectomies may improve the five-year survival rate to between 21 and 61.4% in patients with colorectal tumors, provided there is no metastasis in other organs and the patients' health status allows for this kind of surgery.[4-6] The wide variation in reported survival rates reflects not only the absence of clearly defined prognostic criteria but a consensus regarding the appropriate cases that would benefit from a metastasectomy as well. The prognostic factors included in our patient group were age, gender, the localization of the metastatic node, the stage and localization of the primary tumor, the size of the metastatic nodes, lymph node metastases, recurrent metastases, the carcinoembryonic antigen (CEA) levels, and the disease-free survival rate.[7,8]

In this study, the results of a pulmonary metastasectomy and the prognostic factors in a group of patients with colorectal cancer were evaluated.

PATIENTS AND METHODS

Of the 3,700 patients that underwent surgery between March 1998 and June 2011 in our unit, 440 (11.8%) underwent a thoracotomy for a metastasectomy. However, only 33 (7.5%) patients (17 males and 16 females; median age 55.6 years; range 31-88 years) who underwent a complete pulmonary metastasectomy for the metastasis of colorectal cancer were included in this retrospective study. Those who underwent an incomplete metastasectomy or a metastasectomy for other tumor types were excluded.

Preoperatively, thoracic computed tomography (CT), abdominal CT to assess the primary tumor, and positron emission tomography (PET)-CT to evaluate other possible metastases were performed on all of the patients. In addition, the CEA levels were measured in all of the subjects before the surgery.

In order for a metastasectomy to be performed, all of the patients needed to have the following: a complete resection of the primary tumor with no local recurrence or extra pulmonary metastasis, the presence of appropriate lesions for a complete resection in terms of number and localization, an adequate respiratory reserve, and no comorbidities preventing thoracic surgery. Those who were unable to meet these criteria underwent chemotherapy and radiotherapy and were not included in the study.

The patients were followed up by having a chest X-ray one month after the surgery and undergoing thoracic and abdominal CT every six months as well as a yearly PET-CT examination.

Due to the high proportion of smokers in our study group, the threshold for CEA was set at 5 ng/mL. Disease-free survival was defined as the length of time from the surgery for the primary tumor to the detection of lung metastases, and survival was defined as the period between the diagnosis of lung metastasis and death. We also explored the effects of age, gender, primary tumor localization, CEA levels, recurrence, and disease-free survival with respect to the overall survival and mortality rates of the patients.

Statistical analysis was performed using the PASW Statistics for Windows version 18.0 (SPSS Inc., Chicago, IL, USA) software program. Continuous data was expressed as mean ± standard deviation (SD) when there was normal distribution, and medians were used when the data was not normally distributed. Survival curves were obtained using the Kaplan-Meier product limit estimation method, and the survival curves of different groups were compared using a log-rank test. A p value of below 0.05 was considered to be significant.

RESULTS

The colon was the primary tumor site of in 13 (39%) of the patients while for 20 patients (61%), it was in the rectum. In addition, the CEA concentration was above 5 ng/mL in six patients but was below that level in the other 27. Furthermore, a right-sided thoracotomy was performed on 18 (55%) of the patients, whereas it was left-sided in 14 (42%) others, and bilateral in one (3%). Moreover, the resection was non-anatomic (wedge/precision cautery excision) in 27 (82%) of the patients while six (18%) had a lobectomy due to a centrally localized metastatic lesion (Table 1). No mortality occurred in our study.

A total of 52 metastatic nodules were excised from the 33 patients. Table 2 shows the site of the primary tumor and the number and location of the metastatic nodules as well as the disease-free survival and overall survival rates.

Table 1. Patient characteristics

	n	%	Mean	Range
Age				
≥70	4	12	55.6	31-88
<70	29	88		
Gender				
Male	17	52		
Female	16	48		
Primary tumor				
Rectum	20	61		
Colon	13	39		
Preoperative CEA level				
>5 ng/mL	6	18		
≤5 ng/mL	27	82		
Type of operation				
Lobectomy	6	18		
Non-anatomic resection (wedge or precision)	27	82		
Number of metastases				
Solitary	23	70		
Multiple (bilateral metastasectomy: 1, sequential: 9)	10	30		

CEA: Carcinoembryonic antigen.

Thirteen of our patients (39%) had recurrent disease, and in five of these (15%) it was confined to the lungs. These five subsequently underwent a re-thoracotomy for the metastasectomy. In the other eight patients, chemoradiotherapy was administered due to widespread metastases (Table 2).

The median survival rate for the 33 patients was 74 months (6-99) while the one-, three-, and five-year survival rates were 97%, 79%, and 62%, respectively (Figure 1).

When we divided the patients into two subgroups on the basis of age (≥70 years and <70 years), they did not differ significantly in terms of survival rate 50% and 66% (p=0.952) (Table 3). In addition, the median survival rate for the male patients was 49 months (95% CI 26-72), and the one-, three-, and five-year survival rates were 94%, 70%, and 33%, respectively. For the female subgroup, the median survival rate was 92 months (95% CI, 80-105), and the one-, three-, and five-year survival rates were 100%, 89%, and 89%, respectively. The difference in the overall survival between the genders was statistically significant (p=0.001) (Figure 2).

We also evaluated the patients by dividing them into two subgroups by whether their primary tumor location was the colon or the rectum and found that for 13 (39%), it tumor was in the colon while for the other 20 (61%), it was in the rectum. The median survival rate for the patients with a primary tumor in the colon was 89 months, whereas it was 71 months for those with a rectal tumor. Furthermore, the five-year survival rates in the colon subgroup was 86%, and in the rectum subgroup, it was 51%, (p=0.057) (Table 3).

A pre-thoracotomy CEA level of below 5 ng/mL was associated with the 100%, 89%, and 75% survival rates at one-, three-, and five-years, respectively, whereas the corresponding figures for those with a CEA level above 5 ng/mL were 83%, 42%, and 0% (p=0.001) (Figure 3).

The patients with a disease-free interval (DFI) of less than 12 months had a median survival rate of 71 months while those with a DFI of over 12 months had a slightly higher median survival rate of 74 months. However, this difference was not statistically significant (p=0.346). When we divided the patients into subgroups according to whether their DFI was ≤36 months or >36 months [a risk factor in the International Registry of Lung Metastases (IRLM) criteria], no significant differences were noted with regard to the survival rates (p=0.414) (Table 3).

Additionally, we found that the patients with recurrent disease following the pulmonary metastasectomy had a five-year survival rate of 71 months (range 54-86), whereas the corresponding figure for those without a recurrence was 74 months (range 37-110) (p=0.734) (Table 3).

DISCUSSION

Colorectal cancers represent the second most common cause of cancer-associated deaths. Of these patients, 10-20% have lung metastasis, and 2-4% of all lung metastases originate from the colon or rectum. Even with chemotherapy, five-year survival rates in cases involving lung metastasis of colorectal cancer are very low (<5%), with complete resection being regarded as a potential curative treatment for these patients.[9-11] As previously mentioned, there have been wide variations in the reported survival rates, and this has led to a continuing debate concerning the prognostic factors responsible for these differences. Some of the potential prognostic factors cited in earlier studies included age, gender, the number of metastatic nodules, the extent of metastases, disease-free survival, the CEA levels, mediastinal lymph node involvement, the presence of extrathoracic metastases, and recurrence,[8,13] and of these, CEA is generally considered to be an important prognostic marker in primary colorectal cancer, with elevated follow-up levels being suggestive

Table 2. Carcinoembryonic antigen levels and the follow-up data of the patients who underwent a metastasectomy

No	Age/gender (years)	Localization of primary tumor	Pre-thoracotomy CEA level (ng/mL)	DFI (months)	Thoracotomy/ re-thoracotomy	Number of nodules	Status	Follow-up (months)	Relapse
1	55/M	Colon	2.26	134	Left	3	Alive	24	Lung, liver
2	63/M	Rectum	3.60	59	Left/right	2+2	Dead	23	Lung
3	48/F	Rectum	2.32	48	Right	2	Alive	15	–
4	38/F	Rectum	2.21	10	Right	1	Alive	74	Colon
5	64/F	Colon	2.48	13	Right	1	Alive	26	–
6	52/M	Rectum	12.6	25	Right	1	Dead	9	–
7	69/M	Colon	8.50	12	Left	5	Alive	47	Lung, liver
8	65/M	Rectum	3.31	43	Right	1	Alive	9	–
9	72/M	Colon	7.30	49	Left	1	Dead	31	–
10	64/F	Colon	1.42	24	Left	1	Alive	62	Lung, liver
11	59/M	Rectum	4.60	48	Left	1	Alive	59	–
12	44/F	Colon	1.64	6	Right	1	Alive	9	–
13	37/F	Rectum	4.50	44	Bilateral	4	Dead	38	–
14	36/F	Rectum	2.10	30	Left	1	Alive	81	Brain
15	71/M	Rectum	4.54	23	Right/right	1+2	Dead	49	Lung
16	40/M	Rectum	1.28	43	Left	1	Dead	74	–
17	52/M	Colon	4.43	51	Left	2	Alive	51	Brain, mediastinum
18	47/F	Colon	3.60	2	Left	1	Alive	24	–
19	76/F	Colon	1.40	36	Left	1	Alive	95	–
20	52/F	Rectum	1.46	23	Right	1	Alive	15	–
21	60/F	Colon	0.70	8	Left	1	Alive	82	–
22	64/F	Rectum	1.70	23	Right/right	1+1	Alive	90	Lung
23	55/M	Rectum	2.99	12	Right	1	Alive	10	–
24	88/F	Colon	2.28	31	Right	1	Alive	99	–
25	67/M	Rectum	3.56	0	Right	1	Alive	20	–
26	57/M	Rectum	8.15	13	Right	1	Dead	24	–
27	50/F	Colon	2.09	48	Left	1	Alive	84	–
28	53/M	Rectum	3.40	16	Right/right	2+2	Dead	71	Lung, colon
29	51/M	Colon	4.50	28	Right	1	Dead	60	Lung, mediastinum
30	51/F	Rectum	3.80	75	Left/right	1+1	Alive	23	Lung
31	31/M	Rectum	3.20	0	Right/left	3+1	Dead	49	Lung
32	48/F	Rectum	2.18	84	Right	4	Alive	6	–
33	58/M	Rectum	4.74	5	Right	2	Alive	14	–

CEA: Carcinoembryonic antigen; DFI: Disease free interval.

of metastasis. On the other hand, the prognostic significance of CEA in candidates for thoracotomies due to lung metastases of colorectal cancer has not been clearly defined. In a multicenter study conducted between 1972 and 2002 that involved 128 cases in which CEA levels of between 2.5 and 7 ng/mL were accepted as normal, Inoue et al.[2] determined that the patients with normal CEA levels had a significantly higher five-year survival rate (51.9%) than those with higher CEA levels (38.3%) (p=0.0184). Similarly, in a study by Rena et al.[10] analyzing 80 patients, the five-year survival rate was also higher in the patients with normal CEA levels (58.2% vs. 0%) (p=0.0001).

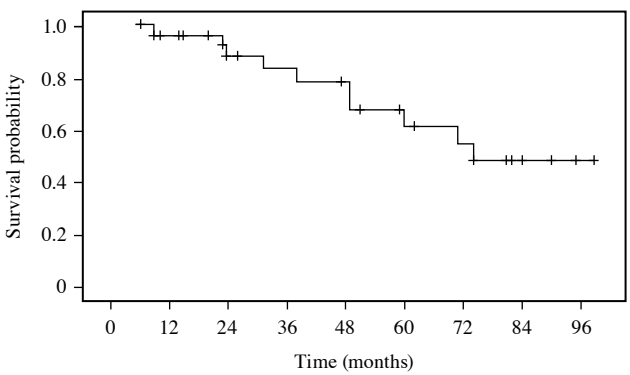

Figure 1. Overall survival rate.

In addition, Rama et al.[12] reported a five-year survival rate of 61% following resection in patients with normal CEA levels, whereas the corresponding five-year survival and median survival rates for those with elevated CEA levels were 19% and 21 months, respectively. Moreover, in a 10-year study by Lee et al.,[14] CEA levels of more than 5 ng/mL were associated with poorer survival (p=0.001).

Table 3. Correlation between age, gender, primary tumor localization, disease-free intervals, pre-thoracotomy carcinoembryonic antigen levels, and recurrence and the patient survival rates

	Number of patients	Five-year survival rate (%)	*p*
Age			
≤70	29	66	0.952
>70	4	50	
Gender			
Male	17	33	**0.001**
Female	16	89	
Primary tumor			
Rectum	20	51	0.057
Colon	11	86	
Disease free interval (month)			
≤12	11	67	0.354
>12	22	60	
Pre-thoracotomy CEA level			
≤5 ng/mL	27	75	**0.001**
>5 ng/mL	6	0	
Recurrence			
Present	13	53	0.734
Absent	20	73	

CEA: Carcinoembryonic antigen.

Furthermore, in a review by Warwick ad Page[15] entitled, a pre-thoracotomy CEA level of higher than 5 ng/mL was associated with a five-year survival rate of 22.7%, whereas it was 48.3% for those with normal CEA levels.

Our findings were at odds with the reports that have hypothesized that preoperative CEA levels have no prognostic significance, but they support those authors who attributed some prognostic significance to these levels.[16-21]

The majority of the studies conducted on this patient population have reported that gender had no effect on the prognosis. In the study by Riquet et al.,[22] the median survival rates for female and male patients were 38 and 48 months, respectively (p=0.17), and Pfannschmidt et al.[23] reported a rate of 40 months in female patients and 39.6 months in the males. In addition, they determined that the five-year survival rates for the female and male patients were 32.3% and 32.6%, respectively (p=0.98). Similar observations have also been published by Inoue et al.[24] and Chung et al.[25] In contrast, Onaitis et al.[26] observed a higher recurrence risk following pulmonary metastasectomies in male patients but found no significant differences with regard to survival.

If contrast to these studies, we identified a remarkably better median survival rate in our female subjects of 92 months and a five-year survival rate of 89% compared with a median survival rate of 49 months and a five-year survival rate of 33% for our male patients (p=0.001).

Although the 1997 IRLM report determined that a disease-free survival rate of more than 36 months can have a favorable effect on a patient's prognosis, Pfannschmidt et al.[6] reviewed 20 series on this topic and found only two that reported that disease-free survival had an independent effect on prognosis. Furthermore, in the single-center retrospective study by Onaitis et al.[26] that was comprised of 378 cases, they observed that a disease-free survival rate of less than 12 months had a significant effect on their patients' prognoses.

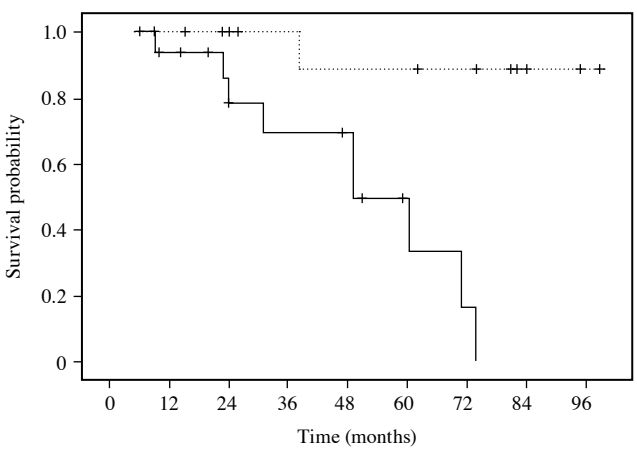

Figure 2. Survival curve by gender. Solid line: Males; Dotted line: Females.

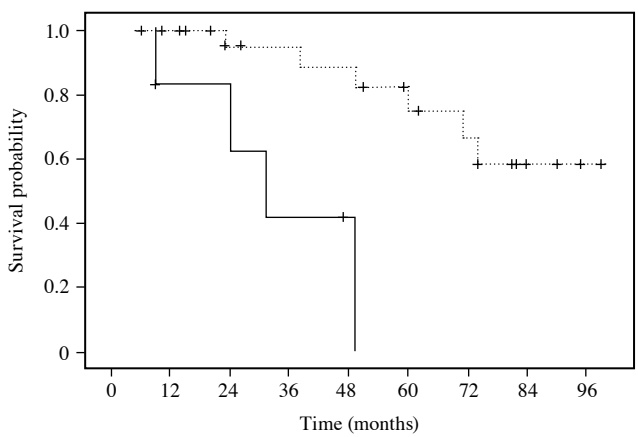

Figure 3. Survival curve by CEA level. Solid line, CEA >5 ng/mL; Dotted line, CEA <5 ng/mL. CEA: Carcinoembryonic antigen.

Table 4. Summary of related publications

References	Study period	Median age	Survival		Predictors of unfavorable prognosis
			Five-year survival rate (%)	Median survival rate (months)	
Inoue et al.[2]	1979-2002	61.8	45.3	49,5	CEA >2 ng/mL, SPT, LM (+), bilateral localization
Headrick et al.[4]	1980-1998	59	30	62	CEA >5 ng/mL, LM (+)
Rena et al.[10]	1980-2000	63	41.1	26,8	DFI <12 months, CEA >5 ng/mL,
Shiono et al.[19]	1992-2002	61	61.4	-	ASFC, VI, LI, PI
Riquet et al.[22]	1985-2007	65	41	-	VI
Onaitis et al.[26]	1998-2007	61	-	-	Gender, DFI <12 months, NOM >3
Pfannschmidt et al.[23]	1985-2000	60.2	48	-	NOM >1
Welter, Essen, 2006[6]	1993-2003	62	39.1	47,2	NOM >5, LM (+), MD >5 cm
Watanabe et al.[20]	1992-2000	61	56	28,3	MD, age, SPT
Saito, Osaka, 2002[6]	1990-2000	61.6	39.6	-	CEA >10 ng/mL, LM (+)
Present study	33(17/16)	55.6	62	74	CEA 5 ng/mL, male sex

CEA: Carcinoembryonic antigen; SPT: Stage of the primary tumor; LM: Lymph node metastasis; DFI: Disease free interval; ASFC: aerogenous spread with floating, cancer cell clusters; VI: Vascular invasion; LI: Lymphatic invasion; PI: Pleural invasion; NOM: Number of metastases; MD: Maximum diameter.

In our study, the patients with a disease-free survival rate of less than 12 months had a survival for 71 months on average, whereas those with a disease-free interval of more than 12 months survived for 74 months (p=0.346). Similarly, our patients, with an median disease-free survival rate of <36 months had an overall survival rate of 74 months, whereas the overall survival rate was 76 months for those with a median disease-free interval of ≥36 months (p=0.414).

Studies that have examined the effect of the primary tumor site with regard to survival after a pulmonary metastasectomy have generally reported no differences between colon and rectal tumors, and they found five-year survival rate in patients who undergo a pulmonary metastasectomy due to colon or rectal cancer of 86% and 51%, respectively (p=0.057).[2,6,14,27]

Local recurrence or new metastases following metastasectomies can conceivably affect the prognosis adversely, at least in an indirect manner through the increased morbidity and/or mortality associated with re-thoracotomies. However, contrary to what one might expect and similar to our results, many studies have found no association between recurrences and significant differences in survival rates.[14,16-17,22,28-30] The various views expressed by different authors and the study center comparisons are shown in Table 4.

Conclusion

Although our study provides evidence to support other authors who have suggested that CEA levels significantly affect lung metastasis of colorectal cancer, our findings with respect to the effect that gender has on the prognosis is at odds with many previous reports. Therefore, multicenter studies involving larger sample sizes are needed to better define the prognostic role that gender plays in this patient group and to more clearly delineate the CEA threshold levels associated with poor survival.

Declaration of conflicting interests

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REFERENCES

1. Regnard JF, Grunenwald D, Spaggiari L, Girard P, Elias D, Ducreux M, et al. Surgical treatment of hepatic and pulmonary metastases from colorectal cancers. Ann Thorac Surg 1998;66:214-8.
2. Inoue M, Ohta M, Iuchi K, Matsumura A, Ideguchi K, Yasumitsu T, et al. Benefits of surgery for patients with pulmonary metastases from colorectal carcinoma. Ann Thorac Surg 2004;78:238-44.
3. Şengül AT, Başoğlu A, Büyükkarabacak YB, Yetim TD, Kutlu T. Metastatik akciğer tümörlerinin tedavisinde metastazektomi ve prognostik faktörlerin değerlendirilmesi. Turk Gogus Kalp Dama 2009;17:87-91.
4. Headrick JR, Miller DL, Nagorney DM, Allen MS,

Deschamps C, Trastek VF, et al. Surgical treatment of hepatic and pulmonary metastases from colon cancer. Ann Thorac Surg 2001;71:975-9.
5. Kanzaki R, Higashiyama M, Oda K, Fujiwara A, Tokunaga T, Maeda J, et al. Outcome of surgical resection for recurrent pulmonary metastasis from colorectal carcinoma. Am J Surg 2011;202:419-26.
6. Pfannschmidt J, Dienemann H, Hoffmann H. Surgical resection of pulmonary metastases from colorectal cancer: a systematic review of published series. Ann Thorac Surg 2007;84:324-38.
7. Welter S, Jacobs J, Krbek T, Krebs B, Stamatis G. Long-term survival after repeated resection of pulmonary metastases from colorectal cancer. Ann Thorac Surg 2007;84:203-10.
8. Hirosawa T, Itabashi M, Ohnuki T, Yamaguchi N, Sugihara K, Kameoka S, et al. Prognostic factors in patients undergoing complete resection of pulmonary metastases of colorectal cancer: a multi-institutional cumulative follow-up study. Surg Today 2013;43:494-9.
9. Hermanek P Jr, Wiebelt H, Riedl S, Staimmer D, Hermanek P. Long-term results of surgical therapy of colon cancer. Results of the Colorectal Cancer Study Group. Chirurg 1994;65:287-97. [Abstract]
10. Rena O, Casadio C, Viano F, Cristofori R, Ruffini E, Filosso PL, Maggi G. Pulmonary resection for metastases from colorectal cancer: factors influencing prognosis. Twenty-year experience. Eur J Cardiothorac Surg 2002;21:906-12.
11. Friedel G, Pastorino U, Buyse M, Ginsberg RJ, Girard P, Goldstraw P, et al. Resection of lung metastases: long-term results and prognostic analysis based on 5206 cases-the International Registry of Lung Metastases. Zentralbl Chir 1999;124:96-103.
12. Rama N, Monteiro A, Bernardo JE, Eugénio L, Antunes MJ. Lung metastases from colorectal cancer: surgical resection and prognostic factors. Eur J Cardiothorac Surg 2009;35:444-9.
13. Gonzalez M, Poncet A, Combescure C, Robert J, Ris HB, Gervaz P. Risk factors for survival after lung metastasectomy in colorectal cancer patients: a systematic review and meta-analysis. Ann Surg Oncol 2013;20:572-9.
14. Lee WS, Yun SH, Chun HK, Lee WY, Yun HR, Kim J, et al. Pulmonary resection for metastases from colorectal cancer: prognostic factors and survival. Int J Colorectal Dis 2007;22:699-704.
15. Warwick R, Page R. Resection of pulmonary metastases from colorectal carcinoma. Eur J Surg Oncol 2007;33 Suppl 2:S59-63.
16. Melloni G, Doglioni C, Bandiera A, Carretta A, Ciriaco P, Arrigoni G, et al. Prognostic factors and analysis of microsatellite instability in resected pulmonary metastases from colorectal carcinoma. Ann Thorac Surg 2006;81:2008-13.
17. Moore KH, McCaughan BC. Surgical resection for pulmonary metastases from colorectal cancer. ANZ J Surg 2001;71:143-6.
18. Ike H, Shimada H, Ohki S, Togo S, Yamaguchi S, Ichikawa Y. Results of aggressive resection of lung metastases from colorectal carcinoma detected by intensive follow-up. Dis Colon Rectum 2002;45:468-73.
19. Shiono S, Ishii G, Nagai K, Yoshida J, Nishimura M, Murata Y, et al. Histopathologic prognostic factors in resected colorectal lung metastases. Ann Thorac Surg 2005;79:278-82.
20. Watanabe I, Arai T, Ono M, Sugito M, Kawashima K, Ito M, et al. Prognostic factors in resection of pulmonary metastasis from colorectal cancer. Br J Surg 2003;90:1436-40.
21. Kobayashi K, Kawamura M, Ishihara T. Surgical treatment for both pulmonary and hepatic metastases from colorectal cancer. J Thorac Cardiovasc Surg 1999;118:1090-6.
22. Riquet M, Foucault C, Cazes A, Mitry E, Dujon A, Le Pimpec Barthes F, et al. Pulmonary resection for metastases of colorectal adenocarcinoma. Ann Thorac Surg 2010;89:375-80.
23. Pfannschmidt J, Muley T, Hoffmann H, Dienemann H. Prognostic factors and survival after complete resection of pulmonary metastases from colorectal carcinoma: experiences in 167 patients. J Thorac Cardiovasc Surg 2003;126:732-9.
24. Inoue M, Kotake Y, Nakagawa K, Fujiwara K, Fukuhara K, Yasumitsu T. Surgery for pulmonary metastases from colorectal carcinoma. Ann Thorac Surg 2000;70:380-3.
25. Chung CC, Hsieh CC, Lee HC, Wu MH, Huang MH, Hsu WH, et al. Accuracy of helical computed tomography in the detection of pulmonary colorectal metastases. J Thorac Cardiovasc Surg 2011;141:1207-12.
26. Onaitis MW, Petersen RP, Haney JC, Saltz L, Park B, Flores R, et al. Prognostic factors for recurrence after pulmonary resection of colorectal cancer metastases. Ann Thorac Surg 2009;87:1684-8.
27. Tada T, Watanabe T, Kazama S, Kanazawa T, Hata K, Komuro Y, et al. Reduced p16 expression correlates with lymphatic invasion in colorectal cancers. Hepatogastroenterology 2003;50:1756-60.
28. Welter S, Jacobs J, Krbek T, Poettgen C, Stamatis G. Prognostic impact of lymph node involvement in pulmonary metastases from colorectal cancer. Eur J Cardiothorac Surg 2007;31:167-72.
29. Nagakura S, Shirai Y, Yamato Y, Yokoyama N, Suda T, Hatakeyama K. Simultaneous detection of colorectal carcinoma liver and lung metastases does not warrant resection. J Am Coll Surg 2001;193:153-60.
30. Treasure T, Fallowfield L, Farewell V, Ferry D, Lees B, Leonard P, et al. Pulmonary metastasectomy in colorectal cancer: time for a trial. Eur J Surg Oncol 2009;35:686-9.